

1.825. Applicants also request a one month extension of time for response under 37 C.F.R. 1.136 (a) and enclose the required fee pursuant to 37 C.F.R. 1.17 (a)(1).

A Sequence Listing in computer readable format has not previously been filed in this application. Applicants submit herewith an initial copy of the Sequence Listing in computer form and a substitute copy of the Sequence Listing in paper form.

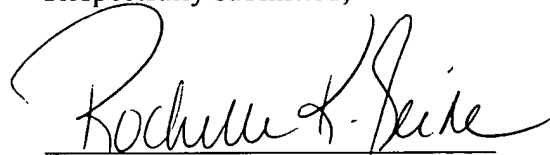
Rewritten paragraphs appear in the preceding "IN THE SPECIFICATION" section. Attached hereto is a marked-up version of the changes made to the specification paragraphs by the instant amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE" and is only included for the Examiner's convenience. Should any discrepancies be discovered, the version presented in the preceding "IN THE SPECIFICATION" section shall take precedence.

The content of the paper and computer readable copies of the Sequence Listing submitted in accordance with 37 C.F.R. §1.821(c) and (e) are the same and do not include new matter.

PATENT

Applicants enclose the fee required for a one month extension of time in accordance with 37 C.F.R. 1.136 (a) and enclose the required fee pursuant to 37 C.F.R. 1.17 (a)(1). However, please charge any fees associated with this filing or credit any overpayment to Deposit Account No. 02-4377. Two copies of this paper are enclosed. Applicants also enclose a copy of the Notice of Incomplete Reply.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADEIN THE SPECIFICATION

The Brief Description of the Drawings beginning at page 11, line 23 and ending at page 12, line 4 has been amended as follows:

Figure 5*Nuclease sensitivity mapping of TNF- α 3'UTR- α EP RNA*

5' End-labeled 3'UTR- α EP RNA was digested with T1, U2 or V1 nuclease directly to assay structure (*str*) (*c*, without nuclease) and, for T1 and U2, also after denaturation at 50°C in 7 M urea (*seq*). Nucleotide ladder was generated by alkaline hydrolysis (OH). Autoradiogram of sequencing gel is shown (Fig. 5A). Stem and loop regions relate to secondary structure at right, showing sites of nuclease attack, based on multiple analyses. GGGC is from plasmid. 2-APRE is the 2-AP response element (SEQ ID NO. 7) (Fig. 5B). Phylogenetic conservation of sequences is shown for *Homo sapiens* (human) (SEQ ID NO. 8), *Sus scrofa* (wild boar) (SEQ ID NO. 9), *Oryctolagus cuniculus* (rabbit) (SEQ ID NO. 10), *Bos taurus* (bull) (SEQ ID NO. 11) and *Capra hircus* (goat) (SEQ ID NO. 12) (Fig. 5C).

The Detailed Description of Preferred Embodiments on page 15 lines 10-19 has been amended with the following paragraph:

SEQ ID NO:1, SEQ ID NO:5, SEQ ID NO:2 and SEQ ID NO:6 are shown in the following Table 1.

Table 1

SEQ ID NO:1 (upper strand) and SEQ ID NO:5 (lower strand)

GAATTCAAACCTGGGGCCTCCAGAACTCACTGGGGCCTACAGCTTTGATCCCTGACATCTG
 2817-----+-----+-----+-----+-----+-----+2876
 CTTAAGTTTGAACCCCGGAGGTCTTGAGTGACCCCGGATGTCGAAACTAGGGACTGTAGAC

 GAATCTGGAGACCAGGGAGCCTTTGGTTCTGGCCAGAATGCTGC
 2877-----+-----+-----+-----+-----+-----2920
 CTTAGACCTCTGGTCCCTCGGAAACCAAGACCGGTCTTACGACG

SEQ ID NO:2 (upper strand) and SEQ ID NO:6 (lower strand)

TCAAACCTGGGGCCTCCAGAACTCACTGGGGCCTACAGCTTTGA
 2821-----+-----+-----+-----+-----+-----2863
 CTTAAGTTTGAACCCCGGAGGTCTTGAGTGACCCCGGATGTCGA

The following paragraph in the Detailed Description of Preferred Embodiments beginning on page 23, line 26, and ending on page 24, line 9 has been amended as follows:

pTNF- α (Δ 3'UTR-i3EP) was constructed by joining SphI-digested pTNF- α (Δ 3'UTR) DNA to the 333-bp SphI-SphI TNF- β gene fragment described above which is comprised of 153 terminal bp of the 3'-UTR, the polyadenylation site and downstream

sequences. This plasmid was then digested with XhoI which cuts uniquely inside TNF- α intron 3. A 2-APRE DNA fragment abutted by XhoI restriction sites was then inserted into this site. The 2-APRE DNA fragment was obtained by polymerase chain reaction using pTNF- α DNA as template and two synthetic DNA primers of sequences 5'-CCGCTCGAGAATTCAAACCTGGGGCCTCC-3' (SEQ ID NO: 3) and 5'-CCGCTCGAGTGCAGCATTCTGGCCAGAACC-3' (SEQ ID NO:4) as 5' and 3' primers, respectively; the DNA product was digested with XhoI before ligation.

Orientation of the 2-APRE insert in pTNF- α (Δ 3'UTR-i3EP) was determined by analysis of DNA fragments generated upon PvuII/PstI digestion.